REMARKS

Claims 19 and 22-31 were pending in this application. Claim 19 has been amended herein to clarify that which the Applicant regards as the invention. Claim 19, as amended, is completely supported by the specification as filed, for example at page 8, lines 14-21 and page 26, lines 13-16. No new matter has been added. Upon entry of the amendments made herein, claims 19 and 22-31 will be pending in the application.

THE INDEFINITENESS REJECTION SHOULD BE WITHDRAWN

Claims 19 and 22-31 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. According to applicable case law, 35 U.S.C. § 112, second paragraph, requires a claim to have a clear and definite meaning when construed in light of the complete patent document. *See Standard Oil v. American Cyanamide Co.*, 227 U.S.P.Q. 293 (Fed. Cir. 1985). Specifically, definiteness turns on whether one of skill in the relevant art would understand the bounds of a claim when read in light of the specification. *See Orthokinetic Inc. v. Safety Travel Chairs, Inc.*, 1 U.S.P.Q.2d 1081 (Fed. Cir. 1986).

In the instant case, the Examiner articulates five separate grounds for why the above recited claims are indefinite and thus allegedly fail to apprise the skilled artisan of the scope of the present claims. The Applicant addresses each in turn below.

First, the Examiner alleges that claim 19 is indefinite. Specifically, the Examiner concludes that it would not be clear to one of skill in the art, reading the specification, whether the population of stress protein-peptide complexes are non-covalently associated with each other, or whether each stress protein is non-covalently associated with a peptide. *See* May 3, 2002 Office Action at 2.

Applicant has amended claim 19 to clarify that the stress protein is non-covalently associated with a peptide.

Second, the Examiner contends that Claim 19 is also indefinite in "that the claim preamble does not relate to the conclusion." May 3, 2002 Office Action at 2. In response, the Applicant has amended Claim 19 to obviate the rejection. Specifically, Applicant has amended Claim 19 so as to recite a "recovered" population of peptides.

Third, the Examiner alleges that claim 19 is also indefinite in that "it is not clear what the metes and bound [sic] of 'amount' is." May 3, 2002 Office Action at 2.

Applicant has amended claim 19 so that it no longer recites "amount." The Applicant respectfully submits that in light of the claim amendment, the indefiniteness rejection based on use of the term "amount" has been obviated and should be withdrawn.

Fourth, the Examiner alleges "low pH" as used in claim 24 is indefinite as the metes and bounds of "low pH" are not clear. The Applicant respectfully disagrees and asserts that "low pH" as used in Claim 24 is definite. As used in the present application, one skilled in the art would understand that low pH means acidic pH, as measured against neutral pH and basic pH. Such meaning would be clear to the skilled artisan as of the filing date of the application.

Finally, the Examiner alleges that use of the phrases "cells have been proliferated in vitro" and "cells have been proliferated in vivo" is ambiguous and renders claims 28 and 29 indefinite. The Applicant respectfully disagrees because the specification makes clear the meaning of such phrases, and directs the Examiner's attention to page 16 of the specification, lines 27- 34. The specification teaches

> excised tumor tissue may be proliferated using techniques well known in the art prior to the isolation of the stress protein-peptide complexes. For example, the excised tumor tissue may be proliferated either in vivo, for example, by transfecting a nude mouse with a sample of the tumor tissue, or in vitro, for example, by serially passaging the tumor cells in culture.

Further, various techniques for proliferating tumor tissue were well known in the art at the time of the invention. Accordingly, the Applicant submits that one of skill in the art reading the specification would be apprised of the full scope of the claims, and thus the rejection should be withdrawn.

THE ENABLEMENT REJECTION SHOULD BE WITHDRAWN

Claims 19 and 22-31 stand rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which, allegedly, is only partially enabled. Specifically, the Examiner states, "the specification, while being enabling for heat shock proteins 70, 90, gp96, does not reasonably provide enablement for stress-proteins in general." May 3, 2002 Office Action at 3.

In response, the Applicant respectfully submits that the Examiner has not met the necessary burden that the Patent and Trademark Office bears in establishing a *prima facie* case of non-enablement. A patent applicant's specification which contains a teaching of how to make and use the invention must be taken as enabling unless there is reason to doubt the objective truth of the teachings which must be relied on for enabling support. *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (CCPA 1971)(emphasis added); *see also* MPEP § 2164.02.

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Teletronics Inc.*, 8 U.S.P.Q.2d 1217 (Fed. Cir. 1988).

Case law interpreting what constitutes "undue experimentation" underscores the actuality that experimentation which is complex is not necessarily undue, "if the art typically engages in such experimentation." *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (U.S. Int'l Trade Comm. 1983), *aff'd sub nom., Massachusetts Institute of Technology v. AB Fortia*, 227 U.S.P.Q. 428 (Fed. Cir. 1985). Undue experimentation then, is experimentation that requires a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover*, 170 U.S.P.Q. 276 (CCPA 1971).

Factors to be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. It should be noted that while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. *In re Angstadt*, 190 U.S.P.Q. 214, 219 (C.C.P.A. 1976).

Furthermore, while 35 U.S.C. § 112, first paragraph requires the full scope of the claims to be enabled, the law does not require the scope of enablement provided by the specification to mirror precisely the scope of protection sought by the claims. *See In re Fisher*, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970); *see also In re Wright*, 27 U.S.P.Q.2d 1510

(Fed. Cir. 1993). To be enabled, all the law requires is that the scope of enablement provided by the specification bear a "reasonable correlation" to the scope of the claims. *Id.* The burden of proving that the enabled examples do not reasonably correlate with the scope of the proposed claims is on the Examiner. Furthermore, even if evidence to doubt the proposed correlation exists, "the examiner must weigh the evidence for and against correlation and decide whether one skilled in the art would accept the model as reasonably correlating to the condition." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995). Thus, to support a non-enablement rejection, the Examiner bears the burden of "evaluat[ing] all the facts and evidence and stat[ing] why one would not expect to be able to extrapolate that one example across the entire scope of the claims." *Id.*

The Full Scope of the Present Claims is Enabled by the Specification

The Applicant respectfully submits that the standard of reasonable correlation of enablement has been met in this case and consequently, that the full scope of the present claims is enabled by the specification. Specifically, one of skill in the art would be able to extrapolate the examples provided in the specification for hsp70, hsp90 and gp96, to other stress proteins of the present claims.

The Examiner alleges that while the specification is enabling for heat shock proteins 70, 90 gp96, the specification does not provide enablement for stress-proteins in general. Specifically, the Examiner quotes from Srivastava 1993, (Reference DK), stating that "not all hsps are equivalent in their ability to exert their antigen presenting properties", and thereby concludes that it is "not predictable if all stress proteins are associated with peptides, and secondly [it is not predictable] whether a population of peptides can be obtained from them by the same methods." May 3, 2002 Office Action at 3.

The Applicant respectfully points out that the section of Srivastava 1993 from which the Examiner quotes, compares the antigen presenting properties of two heat shock proteins which the Examiner has already acknowledged are enabled by the specification, hsp70 and gp96. Additionally, the Applicant respectfully submits that the lack of equivalence in the antigen-presenting properties of hsp70 and gp96 would not undermine the predictability that stress proteins generally are associated with peptides and that compositions comprising the peptides are obtainable by the claimed methods.

Moreover, the Applicant respectfully submits that contrary to the Examiner's argument, it is indeed predictable that a population of peptides can be obtained from the stress protein-peptide complexes of the invention by the methods disclosed in the specification.

The Applicant directs Examiner's attention to page 17, lines 5-12 of the specification, wherein stress proteins, as used in the instant application, are defined.

> Stress proteins useful in the practice of the instant invention may be defined as any cellular protein that satisfies the following criteria. It is a protein whose intracellular concentration increases when a cell is exposed to a stressful stimuli, is capable of binding other proteins or peptides, and is capable of releasing the bound proteins or peptides in the presence of adenosine triphosphate (ATP) or low pH.

Specification, page 17, lines 5-12.

Thus the specification teaches that the stress proteins of the invention must be proteins "capable of associating" with other proteins or peptides and secondly, that a population of peptides may be obtained from the stress protein-peptide complexes since the stress proteins are both capable of binding other proteins or peptides and are capable of releasing the bound proteins or peptides in the presence of ATP or low pH. Applicant has provided ample enabling support for the claimed invention.

Additionally, the Examiner alleges that "one of skill in the art would not be able to practice the claimed invention without undue burden, as one of skill in the art is not given sufficient [sic] in the specification as to all the stress proteins that are available in the general scheme of biological systems and the stresses that are imposed upon them, leading to their induction." May 3, 2002 Office Action at 3.

In response, the Applicant respectfully maintains that for the full scope of the present claims to be enabled, the Applicant need not set forth "all the stress proteins that are available in the general scheme of biological systems". All the law requires is that the proposed claims bear a "reasonable correlation" to the examples. As demonstrated above, a skilled artisan would be guided by the specification's disclosure which conveys that a stress protein of the present invention is necessarily a protein whose intracellular concentration increases in response to known stress stimuli, is capable of binding other proteins or peptides and is capable of releasing the bound proteins or peptides in the presence of ATP and/or low pH.

Furthermore, the Applicant respectfully asserts that the specification provides considerable guidance as to stressful stimuli which can induce the stress proteins of the present invention. The Applicant invites the Examiner's attention to page 6, lines 29-32 of the specification wherein various such stressful stimuli are enumerated. Specifically, "heat shock, nutrient deprivation, metabolic disruption, oxygen radicals and infection with intracellular pathogens" are all recited as examples of such stressful stimuli. stress stimuli which may result in an increased intracellular concentration of stress proteins.

The Applicant submits that the skilled molecular biologist or immunologist, enlightened by the teachings of the present specification would be more than capable of routinely generating the compositions of peptides recited in the present claims.

Accordingly, the Applicant requests the rejection of claims 19 and 22-31 be reconsidered and withdrawn.

CONCLUSION

The Applicant respectfully requests that the amendments and remarks of the present response be entered and made of record in the instant application. Claims 19 and 22-31 fully meet all the statutory requirements for patentability. Withdrawal of the Examiner's rejections and early allowance and action for issuance are respectfully requested.

Respectfully submitted,

Date August 5, 2002

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Adriane M. Antler (Reg. No.)
PENNIE & EDMONDS LLP
1155 Avenue of the Americas
New York, New York 10036-2711
(212) 790-9090

Enclosure

EXHIBIT A
MARKED-UP VERSION OF THE CLAIMS AS AMENDED HEREIN
U.S. PATENT APPLICATION NO. 09/657,722

19. (Amended) A composition comprising [an amount of a purified] a recovered population of peptides in admixture with a pharmaceutically acceptable non toxic carrier, wherein said [purified] recovered population of peptides is produced by a method comprising the steps of:

(a) purifying a population of [non-covalently associated] stress protein-peptide complexes from mammalian tumor cells, wherein the stress protein is non covalently associated with the peptide in said complexes;

(b) releasing the peptides from said population of complexes to produce a released population of peptides; and

(c) recovering the released population of peptides.